

The physics and chemistry of directional freezing: implications in biofabrication and cryobiology

Francisco M. Fernandes

Laboratoire de Chimie de la Matière Condensée de Paris, UMR7475, Sorbonne Université
francisco.fernandes@sorbonne-universite.fr

Freezing is ubiquitous in nature. In oceans, rivers, soils, and in the atmosphere, ice is formed under radically different environmental conditions that depend on hydration, temperature and pressure. In most of these conditions freezing threatens the integrity and the viability of biological entities. Paradoxically, cryopreservation (*i.e.* freezing biological entities under strictly controlled conditions) is the only solution to extend the lifespan of living cells, and to preserve biomolecules. In this lecture I will focus on the interaction between biological matter (from biopolymers up to living mammalian cells) with a controlled freezing front¹.

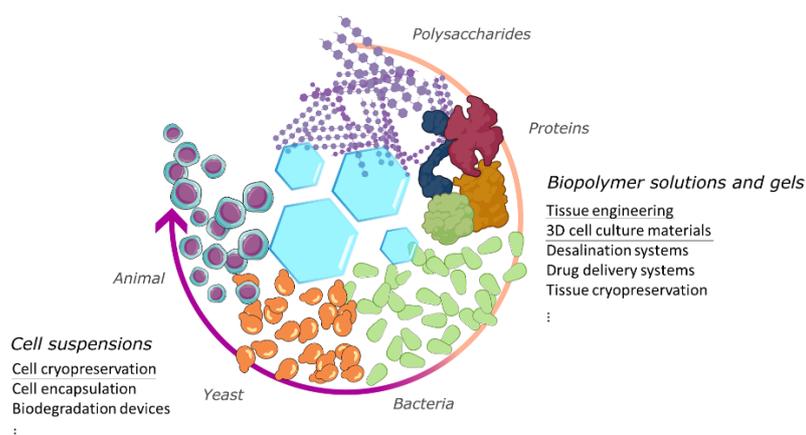


Figure 1: Directional freezing serves as a structuring strategy to manipulate biological entities, allowing to obtain macroporous biomaterials relevant in tissue engineering and 3D cell culture systems. When applied to cell containing media, directional freezing is a powerful strategy to cryopreserve living entities such as mammalian cells without toxic cryoprotectants.

During freezing, ice growth induces a phase separation between pure ice crystals, and the remaining solutes and suspended particles. This strategy can serve as a driving force to design biomimetic systems such as vascular tissue grafts^{2,3}, muscle tendon junctions⁴ as well as 3D cell culture systems⁵. Our recent results in designing biomaterials from the main components of the Extracellular Matrix such as type I collagen using ice will be addressed in the first part of the seminar. The second part will be devoted to the role of directional freezing as an alternative approach to cryopreservation of cells, from model organisms like yeast and bacteria⁶ to cells relevant in human cell therapy⁷ in absence of toxic components such as DMSO. Overall, we demonstrate the potential of controlled freezing processes to outperform current cryopreservation methods and tackle tissue engineering challenges.

References

- ¹Qin et al. *J. Mater. Chem. B* **2021** 9, 889–907.
- ²Martinier et al. *Chem Soc Rev* **2025**, 54, 790-82.
- ³Martinier et al. *Biomater. Sci.*, **2024** 12, 3124-3140.
- ⁴Rieu et al. *ACS Appl Mat & Interf.*, **2019** 11, 14672-14683.
- ⁵Parisi et al. *Biomater. Sci.* **2022**, 10, 6939–6950.
- ⁶Qin et al. *J. Phys. Chem. Lett.* **2020** 11, 7730–7738.
- ⁷Mathieu et al. **2026** *in prep.*